Appendix A. Evidence tables

Author, Year	Purpose, Design	Study size; population	Intervn. group	Control group	Outcome assessed, instruments	Results
Trachtenberg et al.; 2002	Evaluate the effect of abarelix versus treatment with leuprolide + bicalutamide in men with prostate cancer Prospective, randomized controlled, two arms (2:1), non-blinded, multicenter (United States)	N= 255 Inclusion: >18y/o; prostate CA; stage D1 (TxN+Mx) or D2 (TxNxM+), increasing PSA after definitive localized therapy; candidate for neoadjuvant Rx (w/ local or regional disease); candidate for initial course of intermittent hormonal Rx Exclusion: severe bone pain, spinal cord compression, bilateral hydronephrosis, bladder neck obstruction; prior hormonal therapy (except neoadjuvant)	N=170 Abarelix: open label injectable suspension 100 mg (IM) on days 1, 15 (abarelix only), 29, 57, 86, 113, 141 Age range: 51-97, mean 73 ; Rx duration: 24 weeks Baseline testosterone: 119-738, median 341 97% abarelix patients completed treatment to day 85	N=85 Leuprolide + bicalutamide (combined): open label leuprolide acetate 7.5 mg (IM) on days 1, 29, 57, 86, 113, 141 plus 50mg bicalutamide (oral) daily starting on day 1 Age range: 49-93, mean 74 Baseline testosterone: 149-787, median 353 94% combination pts. completed treatment to day 85	Primary end-points: % of patients w/ testosterone>110% of baseline during wk 1 (testosterone surge days 2, 4, and 8); % of pts castrate on day 8; % of pts. maintaining medical castration from days 29 to 85. DHT, FSH, LH and PSA levels assessed at various points Adverse events, allergic reactions, hematological and chemical abnormalities	No patient w/abarelix experienced testosterone surge; 86 % of pts. w/ combination therapy had increased testosterone levels during week 1 ($p<0.001$) 68% of abarelix patients were medically castrated on day 8, vs 0% of control patients (statistical significance not reported); by day 15, 71% of abarelix and 21% of combination patients were castrate. >95% of patients were castrate in both groups on day 29. Achievement and maintenance of castration at day 85 was 92.9% and 95.2% for the abarelix and combination groups respectively. Median percent PSA reduction was similar during the initial 4 wks. (day 15 and day 29). All pts. in both groups had 50% reduction in median PSA compared with baseline on day 169 Safety: overall incidence of adverse events was 93% in abarelix and 95% in combination group; allergic events were observed with similar incidence in both groups but urticaria and pruritus were reported as serious and definitely related to abarelix

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McLeod D et al; 2001	Evaluate the effect of abarelix versus treatment with leuprolide acetate in men with prostate cancer Prospective, randomized control (2:1), non-blinded, multicenter (United States)	N= 269 Inclusion: >18 y/o prostate CA, candidate for neoadjuvant hormonal therapy; metastatic disease (Stage D1 or D2); increasing PSA levels after radical prostatectomy, radiation therapy, or other; serum testosterone level between 220ng/dL and 2 times upper limit of normal Exclusion: severe bone pain, spinal cord compression, bilateral hydronephrosis, bladder neck obstruction; prior hormonal therapy (except neoadjuv.)	N=180 Abarelix: IM injections of abarelix injectable suspension 100 mg injections on days 1, 15 (abarelix only), 29, 57, 86, 113, 141 Age range: 49-88, median 73	N=89 Leuprolide acetate 7.5 mg; injections on days 1, 29, 57, 86, 113, 141 Age range 49-89, median 74	Primary outcome measures: avoidance of testosterone surge; castration on day 8; achievement and maintenance of castration days 29-85 Assessment: days 2, 4, and 8 (testosterone surge); day 8 (rapidity of reduction in testosterone values); days 29-85 (achievement of medical castration) DHT, FSH, LH and PSA levels assessed at various points Adverse events, allergic reactions, clinical laboratory abnormalities	98% abarelix and 95% leuprolide acetate patients completed treatment to day 85 Significantly more leuprolide patients experienced testosterone surge than abarelix patients (82% vs. 0%, $p<0.001$) Significantly more abarelix patients achieved medical castration on day 2, 4, and 8 than leuprolide patients (24%, 57%, and 72% vs. 0% all three days, $p<0.001$) Medical castration at day 85 was achieved and maintained by 91.7% of abarelix patients and 95.5% of leuprolide patients (statistical significance not reported) The percentage change in PSA concentration was significantly greater in abarelix patients than those on leuprolide on days 15 ($p<0.001$) and 29 ($p=0.001$) and was comparable in the two groups after day 29 Safety: overall incidence of adverse events was similar across groups; one event of allergic reaction and one event of increased transaminase were reported as serious and related to abarelix

Author, Year	Purpose, Design	Study size; population	Intervention group	Control group	Outcome assessed, instruments	Results
Koch et al.; 2003.	Study the response to treatment with abarelix of 81 men with advanced prostate cancer symptoms in an open label, single arm (abarelix only) multicenter study	N=81 Eligibility: >18 y/o men with bone pain from skeletal metastases, retroperitoneal adenopathy causing ureteral obstruction, impending neurologic compromise, or an enlarged prostate gland or pelvic mass causing bladder neck outlet obstruction. Exclusion: hormone-refractory disease; hormone therapy in prior 6 months.	IM injections of Abarelix: injectable suspension 100 mg on days 15, 29, 57, 85, 113, and 141 of a 168-day treatment period Median age: 73 y/o; range 40 to 94 y/o. 60/81 patients were treated for at least 24 weeks	No active controlled group	Primary endpoints: Avoidance of bilateral orchiectomy through the first 12 weeks of treatment (through days 29 and 85). Pharmacodynamic endocrine efficacy and PSA levels Secondary endpoints: Change in bone pain intensity; imaging and serologic parameters Urinary tract obstruction, spinal chord compression	69/81 (85%) patients completed 168 days of treatment; two patients withdrew for allergic adverse events. One pt. Withdrew after day 169 following a severe allergic reaction Nine men at one site excluded from efficacy evaluation for regulatory non-compliance. Primary endpoints: 70/72 (97%) men remained in the study and did not require orchiectomy through days 29 and 85. 57/72 (79%) patients had values of 50 ng/dL or less on day 8; 88%, 96%, 97%, 93% of patients achieved this level at days 15, 29, 85, and 169 respectively. PSA levels decreased 75% on average from baseline on day 15 and continued to decrease through day 113. Supportive endpoints: Visual analog scale scores improved between baseline and day 85 in the majority of the 36 patients with bone-related pain completing this test. Overall disease response rate was 88% and 78% on days 85 and 169, respectively. Variable proportions of patients were no longer at risk of spinal chord compression, or required catheters, or had bladder neck obstruction at day 85 compared to baseline. Nine adverse events in 6/81 (7%) of patients were severe and treatment-related.